KCNJ2 gene

potassium voltage-gated channel subfamily J member 2

Normal Function

The *KCNJ2* gene belongs to a large family of genes that produce potassium channels. These channels, which transport positively charged atoms (ions) of potassium out of cells, play key roles in a cell's ability to generate and transmit electrical signals.

The specific function of a potassium channel depends on its protein components and its location in the body. Channels made with the KCNJ2 protein are active in muscles used for movement (skeletal muscles) and heart (cardiac) muscle. In skeletal muscle, these channels play an important role in the pattern of muscle tensing (contraction) and relaxation that allows the body to move. In the heart, the channels are involved in recharging the cardiac muscle after each heartbeat to maintain a regular rhythm. Channels formed with the KCNJ2 protein may also be involved in bone development, but their role in this process is unclear.

Researchers have determined that a molecule called PIP2 must bind to channels made with the KCNJ2 protein for the channels to function normally. PIP2 activates the ion channel and helps it stay open, which allows ions to flow across the cell membrane.

Health Conditions Related to Genetic Changes

Andersen-Tawil syndrome

More than 40 mutations in the *KCNJ2* gene have been identified in people with Andersen-Tawil syndrome, a disorder that causes episodes of muscle weakness (periodic paralysis), changes in heart rhythm (arrhythmia), and developmental abnormalities. Most of these mutations change a single protein building block (amino acid) in the KCNJ2 protein.

Mutations in the *KCNJ2* gene lead to the production of a nonfunctional potassium channel. Some mutations change the shape of the channel so it cannot transport potassium ions, while other mutations prevent the channels from being inserted correctly into the cell membrane. Many *KCNJ2* mutations prevent PIP2 from effectively binding to and activating potassium channels. If the KCNJ2 protein is unable to bind to PIP2, the channels remain closed and potassium ions are unable to flow across the cell membrane. Researchers believe that problems with PIP2 binding are a major cause of Andersen-Tawil syndrome.

A loss of channel function in skeletal and cardiac muscle cells disrupts the normal flow of potassium ions out of these cells, resulting in periodic paralysis and an

irregular heart rhythm. It is not known how mutations in the *KCNJ2* gene contribute to developmental abnormalities of the head, face, and limbs often found in Andersen-Tawil syndrome.

familial atrial fibrillation

At least one mutation in the *KCNJ2* gene is associated with rare cases of familial atrial fibrillation, a form of arrhythmia characterized by uncoordinated electrical activity in the heart's upper chambers (the atria). The identified mutation replaces the protein building block (amino acid) valine with the amino acid isoleucine at position 93 of the KCNJ2 protein (written as Val93Ile or V93I). In cardiac muscle cells, this mutation appears to increase the flow of potassium ions through the channel made with the KCNJ2 protein. The enhanced ion transport may alter the heart's normal rhythm. Researchers are working to determine whether the V93I mutation is a direct cause of familial atrial fibrillation.

short QT syndrome

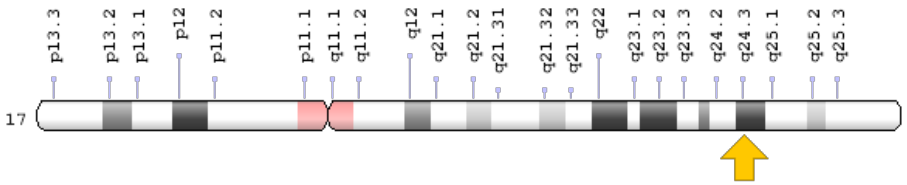
Mutations in the *KCNJ2* gene can also cause a heart condition called short QT syndrome, which is a type of arrhythmia. In people with this condition, the cardiac muscle takes less time than usual to recharge between beats. This change increases the risk of abnormal heart rhythm that can cause fainting or sudden death.

At least two mutations in the *KCNJ2* gene have been found to cause short QT syndrome in a small number of affected families. These mutations change single amino acids in the KCNJ2 protein, which increases the activity of channels made with this protein. As a result, more potassium ions flow out of cardiac muscle cells at a critical time during the heartbeat, which can lead to an irregular heart rhythm.

Chromosomal Location

Cytogenetic Location: 17q24.3, which is the long (q) arm of chromosome 17 at position 24.3

Molecular Location: base pairs 70,169,535 to 70,180,044 on chromosome 17 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- cardiac inward rectifier potassium channel
- HHBIRK1
- HHIRK1
- HIRK1
- inward rectifier K+ channel KIR2.1
- IRK1
- IRK2_HUMAN
- KIR2.1
- LQT7
- potassium channel, inwardly rectifying subfamily J, member 2
- potassium inwardly-rectifying channel J2
- potassium inwardly-rectifying channel, subfamily J, member 2

Additional Information & Resources

Educational Resources

- Biochemistry (fifth edition, 2002): Specific Channels Can Rapidly Transport Ions Across Membranes
  https://www.ncbi.nlm.nih.gov/books/NBK22509/
- Neuromuscular Disease Center, Washington University: KCNJ2 potassium channel
  http://neuromuscular.wustl.edu/mother/chan.html#kcnj2

GeneReviews

- Andersen-Tawil Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1264

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28KCNJ2%5BTIAB%5D%29+OR+%28%28HHBIRK1%5BTIAB%5D%29+OR+%28inward+rectifier+K++channel+KIR2.1%5BTIAB%5D%29+OR+%28IRK1%5BTIAB%5D%29+OR+%28KIR2.1%5BTIAB%5D%29+OR+%28LQT7%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D

OMIM

- POTASSIUM CHANNEL, INWARDLY RECTIFYING, SUBFAMILY J, MEMBER 2
  http://omim.org/entry/600681

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_KCNJ2.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=KCNJ2%5Bgene%5D
- HGNC Gene Family: Potassium voltage-gated channel subfamily J
  http://www.genenames.org/cgi-bin/genefamilies/set/276
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=6263
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/3759
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  http://www.uniprot.org/uniprot/P63252

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